

Boss et al., *J. Biol. Chem.*, 256(24):12958-12961 (1981) discloses isolation of a target yeast iso-1-cytochrome c (CYC1) mRNA by hybridization to a complementary cloned DNA attached to a solid matrix (*e.g.*, diazobenzylmethyl cellulose powder), followed by sequencing using a CYC1-specific oligonucleotide primer and the dideoxy chain termination method. The sequencing reaction produces a multitude of sequences from the target nucleic acid, which are detected by gel separation and autoradiography.

Brown et al., *Ann. Rev. Biochem.* 43:667-693 (1974) discloses methods of isolating nucleic acid sequences by using polynucleotides fixed to insoluble matrices, and the desirability of combining nucleic acid isolation with subsequent amplification. Brown et al., at pages 673-674, discloses DNA purification by using an affinity column in which complementary RNA or DNA molecules are fixed to an insoluble support (*e.g.*, nitrocellulose or cellulose) and circulating the soluble DNA mixture through the affinity column. Brown et al., at page 687, paragraph 2, states that "purification of important structural genes will have to be coupled with some method in which a small amount of a given gene can be increased enormously in amount. After purification has enriched the gene sequence ... the remaining DNA would be amplified hundreds to thousandsfold in amount.... The amplification step might be carried out in vitro by an efficient DNA polymerase, which would replicate faithfully each molecule of DNA many times."

Burgess, "Purification and Physical Properties of *E. coli* RNA Polymerase" in *RNA Polymerase* (Losick and Chamberlin, eds.) (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1976), part 1: 69-100, discloses procedures for purifying RNA polymerases and determining enzyme purity, commonly associated enzymatic contaminants (pages 86-89) and properties of RNA polymerases.

Feinberg et al., *Anal. Biochem.* 132:6-13 (1983) discloses a radiolabeling method that uses random hexamer oligonucleotide primers to initiate non-specific enzymatic reproduction of isolated polynucleotides.

Gaubatz et al., *Biochim. Biophys. Acta*, 825:175-187 (1985) discloses a method of cDNA strand displacement synthesis to amplify mRNA sequences.

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Powell et al., *Cell*, 50:831-840 (1987) discloses capture of poly(A)⁺ RNA from a sample by using oligo(dT)-cellulose chromatography, followed by PCR amplification of cDNA made from the eluted RNA and detection of the amplified products by using radioactively labeled oligonucleotides (see Experimental Procedures on pages 838-839).

Saiki et al., *Nature*, 324: 163-166 (1986), discloses that reduced signals in an assay based on PCR amplification may result from failure to purify target DNA, *i.e.*, "inhibition of the amplification process by cellular debris" (see text spanning page 164, column 2 to page 165, column 1).

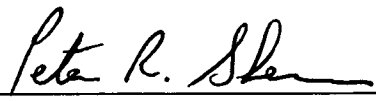
Syvänen et al., *Nuc. Acids Res.*, 14(12):5037-5048 (1986) discloses a hybridization assay in which a target nucleic acid is captured by hybridization to a capture probe with an affinity label (*e.g.*, biotin) and then binds to an affinity matrix (*e.g.*, streptavidin agarose beads) through an affinity interaction (*e.g.*, biotin-avidin interaction). The capture probe and target nucleic acid are hybridized in solution to take advantage of solution-phase kinetics (see pages 5042-5043).

Thompson et al., *Clin. Chem.*, 35(9): 1878-1881 (1989) discloses a hybridization assay that combines reversible target capture, essentially as disclosed in the present reissue application, with enzymatic amplification (PCR) of the purified target nucleic acid.

This information has been served on applicant in accordance with 37 C.F.R. 1.248, as indicated by the attached proof of service.

Respectfully submitted,

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